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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

BLAND, LAYLA D

ART UNIT

PAPER NUMBER

1623

NOTIFICATION DATE

DELIVERY MODE

05/13/2010

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@oshaliang.com
buta@oshaliang.com

Office Action Summary	Application No. 10/519,983	Applicant(s) KAJIHARA, YASUHIRO	
	Examiner LAYLA BLAND	Art Unit 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 2/10/2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,5-7 and 22-25 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,5-7 and 22-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This office action is a response to Applicant's amendment submitted February 10, 2010, wherein claims 1, 5, and 6 are amended and claims 2-4 and 8-21 are canceled.

Claims 1, 5-7, and 22-25 are pending and are examined on the merits herein.

The rejection of claims 1, 5-7, and 22-25 under 35 U.S.C. 103(a) as being unpatentable over Yamamoto in view of Meinojohanns is withdrawn in view of the English translation of the priority document JP2002-349166 (filed November 29, 2002). Yamamoto was published on June 5, 2003, after the priority date.

In view of Applicant's amendment submitted February 10, 2010, the rejection of claims 1, 5-7, and 22-25 under 35 U.S.C. 112, second paragraph, as being indefinite with respect to "under pH 5 to 6" and "at least sugar residues" is withdrawn.

The following rejections are maintained:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 5-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed,

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had possession of the claimed invention. Claim 1 is amended to require the preparation of a protected compound wherein the "benzyl, allyl, or diphenylmethyl group is introduced into the carboxyl group of the sialic acid under a condition of pH 5 to 6."

Applicant states that support for this amendment can be found in paragraph [0141] of the published application. Although paragraph [0141] describes benzyl protection at pH 5 to 6, the examiner was unable to locate support for allyl or diphenylmethyl protection at pH 5-6. The examiner was unable to locate a general description of pH required for protection of sialic acid derivatives, and the recitation pH 5-6 in paragraph [0141] is given as part of the specific conditions used for benzyl protection. This is a new matter rejection.

Response to Arguments

Applicant argues that benzylic and allylic substitutions occur under similar conditions, and that one skilled in the art would reasonably conclude that the inventor possessed the claimed invention with allyl or diphenyl methyl analogs. Applicant's argument has been carefully considered but is not persuasive. As set forth above, the specification does not describe allyl or diphenylmethyl protection at pH 5-6, nor does it contain a general description of protection conditions at pH 5-6. To the contrary, the specification (page 26, lines 17-21) simply states that protection can be conducted in a known manner. The only disclosure of protection at pH 5-6 is given specifically for benzyl protection, and specifically using Cs_2CO_3 , DMF, and benzyl bromide at room temperature. The specification provides no disclosure for protection at pH 5-6 other than the specific example discussed above, and thus the skilled artisan would not

conclude that the inventors had full possession of the claimed invention at the time the application was filed.

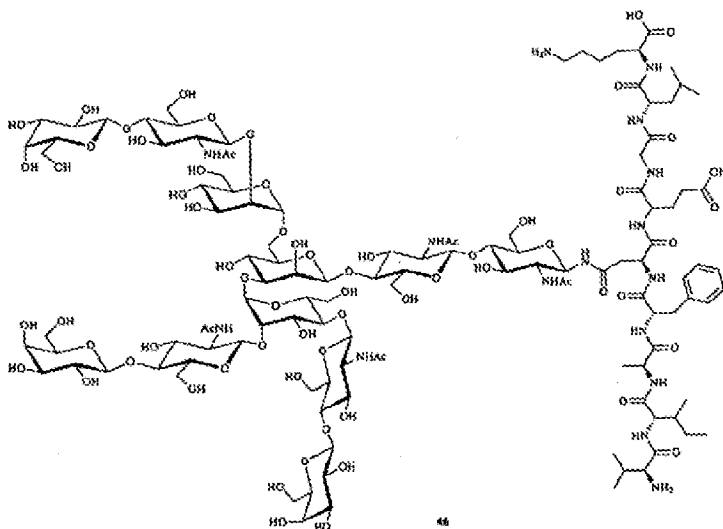
Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 5-7, and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Meinojohanns (J. Chem. Soc. Perkin Trans. I, 1998, pages 549-560, PTO-1449 submitted December 20, 2007) in view of Keil et al. (Angew. Chem. Int. Ed. 2001, 40, No.2, pp. 366-369) and Greene et al. (Protective Groups in Organic Synthesis, Third Edition, John Wiley & Sons, Inc., 1999, pages 415-419).

Meinojohanns teaches a method for preparing asparagine-linked glycopeptides such as the one shown below [page 556, Scheme 5]:



The products can be prepared by attaching an Fmoc-protected amino acid to a resin, followed by deprotection of the Fmoc group and coupling of another amino acid, which is repeated. Then the asparagine building blocks, which are protected with Fmoc as well (see page 555, Scheme 4), are coupled and the peptide synthesis is continued as described above. Both di- and tri-antennary building blocks are taught [page 555, Scheme 4]. Finally, the glycopeptide is cleaved from the resin. [pages 559-560].

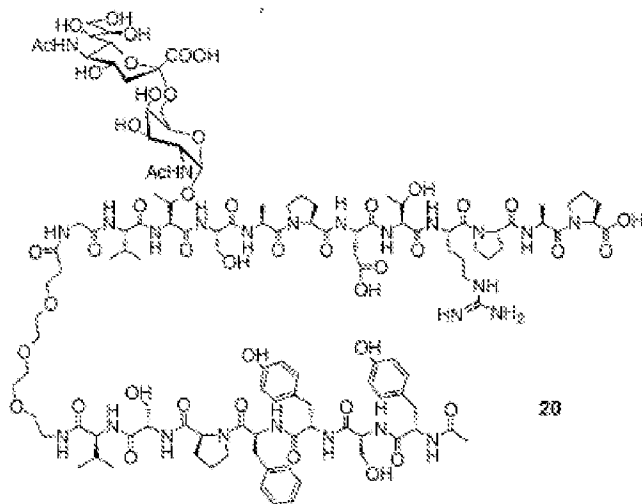
Secreted and cell-surface proteins are glycosylated with both N- and O-linked oligosaccharides, and the effects of the sugars on such properties as immunogenicity is of importance [page 549, first paragraph]. The N-linked glycopeptides prepared by Meinojohanns could be used as substrates for 1-6-sialyltransferase [page 556, scheme 5].

The difference between Meinojohanns' process and the claimed process is that Meinojohanns does not utilize an asparagine building block which contains a sialic acid

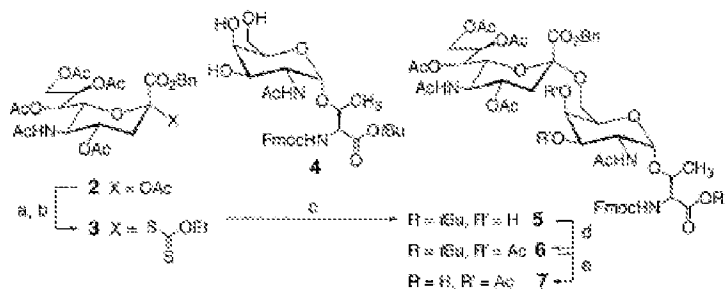
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moiety, but instead suggests the use of sialyltransferase to introduce sialyl moieties into the product.

Keil teaches a process for preparing compound 20, which contains a sialic acid moiety [page 368, Scheme 4].



Compound 20 is prepared by a process which includes preparation of sialic acid-containing building block 7, shown below, which is then used in the solid-phase synthesis of the glycododecapeptide sequence of compound 20 [page 367, Scheme 1].



Scheme 1. a) AcCl , 20°C , 3 d, quant.; b) KCS_2OEt , EtOH , 20°C , 4 h, 73%; c) $\text{CH}_3\text{SBn}/\text{AgOTf}$, $\text{CH}_3\text{CN}/\text{CH}_2\text{Cl}_2$ (2/1), -62°C , 3 h, 60%; d) Ac_2O , pyridine, 0°C , 4 h, 84%; e) $\text{TFA}/\text{CH}_2\text{Cl}_2$ (1/1), anisole, 20°C , 6 h, quant. Ac = acetyl, Tf = trifluoromethanesulfonyl, TFA = trifluoroacetic acid.

The carboxylic acid moiety of sialic acid-containing compounds 2-7 was protected as a benzyl ester, as shown above.

Greene teaches methods for protecting a carboxylic acid as its benzyl ester. In one example, a selective protection is carried out under acidic conditions [page 416, entry 5]. The carboxyl group which is near the amino group is left unprotected, while the other carboxyl group is protected.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to carry out Meinojohanns' process for preparing glycopeptides, using an asparagine building block which contains sialic acid groups. The claimed invention can be seen as an improvement over Meinojohanns' method because the sialyl group is present without requiring additional enzymatic transformation. Keil teaches a method for preparing the sialic acid-containing building blocks, which are coupled to the peptide in the same way that Meinojohanns' building blocks are coupled. Thus, the skilled artisan could prepare sialic acid-containing building blocks for use in Meinojohanns' process, and avoid additional enzymatic transformation. Keil's sialic acid is protected as the benzyl ester. Greene teaches a number of methods for protecting carboxylic acids as the benzyl ester, including one which is carried out under acidic conditions. Greene does not teach the exact pH required to achieve protection, but it is routine in the art for the skilled artisan to optimize reaction conditions for suitability to the particular substrate which is being protected. Thus, the claimed invention is obvious over Meinojohanns in view of Keil and Greene.

Response to Arguments

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies

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(i.e., selective protection of the carboxyl group of sialic acid) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant argues that, under the conditions taught in Greene, various hydroxyl groups would react without selectivity and that Green's conditions are more acidic than pH 5-6. Applicant's arguments with respect to selectivity are not persuasive because selective protection is not required by the claims and because arguments of counsel cannot take the place of factually supported objective evidence. See, e.g., *In re Huang*, 100 F.3d 135, 139-40, 40 USPQ2d 1685, 1689 (Fed. Cir. 1996); *In re De Blauwe*, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984). The burden is shifted to Applicant to show factually supported objective evidence to rebut the prima facie case of obviousness over the prior art. Furthermore, Greene does show a selective protection of a carboxyl group in the presence of a hydroxyl group and in the presence of another carboxyl group which is alpha to an amino group. Applicant's arguments with respect to the acid used in the selective protection are not persuasive because it is routine to optimize reaction conditions for suitability to the particular substrate. Greene's selective protection is an example of acid-catalyzed esterification, as recognized by Applicant, and the skilled artisan is aware of acidic conditions which are required to ionize a carboxyl group for acid-catalyzed esterification. Thus, the skilled artisan would arrive at the claimed conditions using no more than routine optimization of known protection conditions. For these reasons, the rejection is maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAYLA BLAND whose telephone number is (571)272-9572. The examiner can normally be reached on Monday - Friday, 7:00 - 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anna Jiang can be reached on (571) 272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Layla Bland/
Examiner, Art Unit 1623

/Shaojia Anna Jiang/
Supervisory Patent Examiner
Art Unit 1623